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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,914	PERRICONE ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-39 is/are pending in the application.

4a) Of the above claim(s) 27-39 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-26 is/are rejected.

7)☒ Claim(s) 9 and 22 is/are objected to.

8)☒ Claim(s) 1-39 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/29/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges receipt of application 10/749,914 filed on 05/30/03.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-26 are drawn to a carrier composition for transdermal delivery of a macromolecule comprising a phosphotidylcholine component entrapping the macromolecule, classified in class 424, subclass 450.

II. Claims 27-39 are drawn to a method of administering a drug comprising applying to the skin composition containing: an effective amount of the drug and a carrier having a phosphotidylcholine component entrapping the drug wherein the carrier stabilizes the drug at room temperature, classified in class 514, subclass 78.

The inventions are distinct, each from the other because of the following reasons:

Inventions Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the drug carrier of Group I could be used as a food additive.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Claim 1 is generic to a plurality of disclosed patentably distinct species comprising macromolecules entrapped within a phosphatidylcholine component. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Specifically, the Applicant should elect: 1) a specific drug. If the Applicant desires additional components then the Examiner is requesting that Applicant name or completely define additional components.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance,

whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

A telephone call was made to Stephan McNamara on 07/21/05 and Group I invention, claims 1-26, was chosen for examination on the merits. Claims 27-39 are withdrawn from consideration as being drawn to a non-elected invention. An election of species was also required and insulin was chosen.

Claim Objections

Claims 9 and 22 are objected to because of the following informalities: The weight percent totals add up to 101%. The specification (pages 8 and 9) provides support for 53.25% phosphatidylcholine component, 1.00% surfactant, 1.00% lubricant and 0.75% methyl paraben. Water would then constitute 44% not 45%. Appropriate correction is required. The Examiner is interpreting the claim to read 44% w/w water.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, 17 and 18 contain the trademark/trade name E200 and E400. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a type of polyglycol and, accordingly, the identification/description is indefinite.

For the purpose of examination, the Examiner is interpreting polyglycol E200 and polyglycol E400 to mean a polyglycol of 200 molecular weight and a polyglycol of 400 molecular weight as suggested in the specification on pages 6 and 8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 8, 14-16, 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Modi (U.S. Patent No. 6,214,375).

Claim 1 of the instant invention is directed to a carrier composition for transdermal delivery of a macromolecule, comprising a phosphatidylcholine component entrapping said macromolecule, wherein said component stabilizes said macromolecule at room temperature.

Modi claims a liposomal formulation comprising: I) at least one medicinally active ingredient, such as insulin (Claim 5), II) at least three compounds selected from the group consisting of egg phosphatidylcholine, soy phosphatidylcholine... for example, and III) at least two biodegradable polymers selected from the group consisting of copolymers of sucrose and epichlorohydrin, polyethylene glycols, polyvinyl pyrrolidone... for example (Claim 1) thus anticipating instant claims 1, 2, and 14-16. Soy phosphatidylcholine is enriched with polyunsaturated phosphatidylcholine thus reading on instant claim 3. Polyvinyl pyrrolidone is a known hydrophilic lubricant. Lecithins are known as surfactants. Modi anticipates the addition of antifungal/antimicrobial agents such as methyl paraben to the formulation (Column 4, lines 35-39). Modi anticipates the combination of insulin, soy phosphatidylcholine, dipalmitoyl phosphatidylcholine,

polyethylene glycol, polyvinyl pyrrolidone and methyl paraben thus reading on instant claims 6 and 19. Modi describes a swelling the liposomal formulation in water (Column 7, lines 25-34) and forming multilamellar liposome suspensions in water (Column 8, lines 21-25) thus anticipating instant claims 8 and 21.

The invention of Modi is deemed to meet the limitations of instant claims 1-3, 6, 8, 14-16, 19 and 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4, 5, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi et al. (U.S. Patent No. 4,687,661) in view of Patel et al. (U.S. Patent No. 6,294,192).

Kikuchi et al. disclose a general method for the preparation of liposomes derived from egg yolk or soybean phosphatidylcholine with a non-volatile organic solvent, such polyethylene glycol, used alone or in combinations (See: Abstract; Column 2, lines 18-50; and claims 1 and 2, for example). Kikuchi et al. disclose that the proportion of non-volatile organic solvent is preferably about 1 to about 100 parts by weight per party by weight of the membrane components (Column 2, lines 51-55). The drugs that can be

encapsulated into the liposomes include proteins such as insulin (Column 3, linees 55-59).

Kikuchi et al. do not expressly disclose a phosphatidylcholine component comprising 45% w/w phosphatidylcholine, 50% w/w polyglycol E200 and 5% polyglycol E400.

Patel et al. disclose a pharmaceutical composition for the topical/transdermal delivery of therapeutic agents comprised of at least one hydrophobic and at least one hydrophilic surfactant as well as solubilizers and mixtures of solubilizers. (Column 25, lines 15-19 and lines 52-53). Polyethylene glycols of average molecular weight of about 200 to about 6000, with PEG-400 a preferred solubilizing agent, are disclosed (Column 25, lines 15-63). Patel et al. disclose that the typical amount of solubilizer present in the composition will be in the range of about 1% to about 100% by weight (Column 26, lines 12-14).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phosphatidylcholine preparation of Kikuchi et al. with a combination of PEG 200 and PEG 400 as suggested by Patel et al. to produce the instantly claimed invention. The specific w/w ratio of the low molecular weight PEGs to the phosphatidylcholine component in the composition is deemed merely a matter of judicious selection and routine optimization of conventional working conditions, which is well within the purview of one of ordinary skill in the art as suggested by Patel et al. (Column 26, lines 1-2).

One of ordinary skill in the art would have been motivated to do this because addition of the low molecular weight PEG would enhance the solubility of poorly water soluble therapeutic agents (Patel et al. Column 25, lines 15-18).

One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 7, 9, 17, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi et al. in view of Patel et al.

The teachings of Kikuchi et al. and Patel et al. have been fully discussed previously in this Office Action and the discussion there is incorporated herein by reference.

Kikuchi et al. disclose phosphatidylcholine compositions where, for example, the phosphatidylcholine component is comprised of 9.4 g of glycerin and 2.2 g of egg yolk lecithin (total = 11.6 g) and 0.164 g of dicetyl phosphate for a 98.6% by weight phosphatidylcholine component and 1.4% by weight surfactant component (Column 4, lines 33-37). Kikuchi et al. dilute the 98.6% by weight phosphatidylcholine component

solution with 300 ml of a 0.5% aqueous solution of sodium salicylate, a known preservative, to ultimately produce a sodium salicylate encapsulating liposome suspension (Column 4, lines 38-48).

Kikuchi et al. do not expressly disclose a composition comprising 97.25% phosphatidylcholine component, 1.00% w/w surfactant, 1.00% w/w lubricant, and 0.75% w/w methyl paraben. Kikuchi et al. do not expressly disclose diluting the composition to 53.25% w/w phosphatidylcholine component, 1.00% w/w surfactant, 1.00% w/w lubricant, and 0.75% w/w methyl paraben and 44% water.

Patel et al. disclose that hydrophobic surfactants can be in the range of about 1% to about 60% by weight of the hydrophilic surfactant (Column 21, lines 30-31). Patel et al. defines a number of hydrophobic surfactants as oils (Column 9, lines 8-13 and Column 10, lines 1-13; and Table 5, for example). The Examiner is interpreting the addition of such hydrophobic surfactants to mean the addition of a lubricant. Patel et al. further disclose the addition of other additives including preservatives (Column 26, lines 16-21). Methy paraben is one of the most commonly known preservatives and would be immediately envisaged by one of ordinary skill in the art.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the liposome formulation of Kikuchi et al. to comprise the additional hydrophobic surfactant and preservative as provided by Patel et al. in the specified ratios to arrive at the instant invention. One of ordinary skill in the art has the ability to adjust and readily determine the appropriate amounts of materials required for the composition (Patel et al. Column 26, lines 21-23).

One having ordinary skill in the art would have been motivated to do this because Patel et al. disclose improved solubility of therapeutic agents and less greasy pharmaceutical compositions for topical/transdermal delivery of the active agent.

One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 10, 11, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Modi (U.S. Patent No. 6,214,375) in view of Brieva et al. (U.S. Patent No. 5,985,298).

The teachings of Modi have been fully discussed previously in this Office Action and the discussion there is incorporated herein by reference.

Modi does not expressly disclose the addition of a surfactant which is a siloxylated polyether such as; dimethyl, methyl(propylpolyethylene oxide propylene oxide, acetate) siloxane which is Dow Corning Fluid 190 (Specification, page 8).

Brieva et al. disclose cosmetic compositions comprised of non-volatile silicones, such as Dow 190 (a surfactant), for improved long lasting adherence to the skin of cosmetics (Column 1, lines 4-42; Column 3, lines 53-65).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the teaching of Modi, phosphatidylcholine drug carrier composition, with a siloxylated polyether surfactant such as Dow 190, as suggested by Brieva et al. to produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because it would have been desirable to increase the adherence of the drug carrier to the skin for optimal drug delivery (Brieva et al. Column 1, lines 41-42).

One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 12, 13, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Modi (U.S. Patent No. 6,214,375) in view of Chaiyawat et al. (U.S. Patent No. 6,538,061).

The teachings of Modi have been fully discussed previously in this Office Action and the discussion there is incorporated herein by reference.

Modi does not expressly disclose a carrier composition comprised of a silicone fluid lubricant, which contains low viscosity polydimethylsiloxane polymers.

Chaiyawat et al. disclose cosmetic compositions comprised of silicone fluids of low viscosity, less than 100 cSt at 25 °C, which exist as fluids at or near room temperature (Column 10, lines 48-59). The lubricious silicone fluids include polydimethylsiloxane polymers (dimethicone) (Column 10, lines 60-67 and Column 11, lines 1-4). Furthermore, Chaiyawat et al. disclose that such compositions are suitable as hormone carriers (Column 12, lines 35-38 and 66) as well as drug delivery systems for topical administration of medicinal compositions to the skin (Column 12, lines 55-57).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the carrier composition of Modi to include lubricious silicone fluids as suggested by Chaiyawat et al. to produce the instantly claimed invention.

One of ordinary skill in the art would have been motivated to do this because Chaiyawat et al. disclose that the addition of such emollients improves the appearance of the skin, reduces flaking and tends to remain on the surface of the skin (Column 10, lines 60-66). Therefore, by adding silicone fluids not only are the aesthetics of the carrier compound improved from a patient standpoint but also the drug delivery capabilities.

One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Double Patenting

Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/750,390. Although the conflicting claims are not identical, they are not patentably distinct from each other because practice of the method of formulating an insulin composition as claimed in 10/750,390 would produce the instantly claimed product of the instant application. The product made from the method of 10/750,390 is a specie of the genus of products in 10/749,914 thus making the genus obvious. The essential elements and features are set forth in the claims analysis chart below.

Copending Application 10/750,390 Claim Number	Claim elements	Instant Application 10/749,914 Claim Number	Claim elements
1	Insulin entrapped in Phosphatidylcholine (PC) carrier	1, 14 and 15	Stabilized insulin entrapped in PC carrier
2 and 4	Carrier comprises polyglycol and PC	2 and 4	Carrier comprises polyglycol and PC
3	Enriched with polyenyl-PC	3	Enriched with polyenyl-PC
4	Comprises 45% PC* 50% polyglycol E200 5% polyglycol E400	5	Comprises 45% PC 50% polyglycol E200 5% polyglycol E400
5** and 6	See note below	7	97.25% PC solution 1.00% surfactant, 1.00% lubricant 0.75% methyl paraben
6	53.25% PC solution 1.00% surfactant, 1.00% lubricant 0.75% methyl paraben 44% water	6, 8 and 9	53.25% PC solution 1.00% surfactant, 1.00% lubricant 0.75% methyl paraben 44% water
7	Siloxylated ether	10	Siloxylated ether
8	same ether	11	Same ether
9	Silicone fluid	12	Silicone fluid
10	Low viscosity polydimethylsiloxane	13	Low viscosity polydimethylsiloxane
1-4	Described above	16-18	Stable insulin composition comprising 45% PC component 50% polyglycol E200 5% polyglycol E400
1, 2 and 6	Described above	19 and 21	Carrier comprises a surfactant, a lubricant and methyl paraben and water
1-6	Described above	20	97.25% PC solution 1.00% surfactant, 1.00% lubricant 0.75% methyl paraben
1-4 and 6	Described above	22	53.25% PC solution 1.00% surfactant, 1.00% lubricant 0.75% methyl paraben 44% water
1-7	Described above	23	Siloxylated ether
1-8	Described above	24	Same ether
1-9	Described above	25	Silicone fluid
1-10	Described above	26	Low viscosity polydimethylsiloxane

*: A phosphatidylcholine solution makes obvious all phosphatidylcholine solutions including polyenylphosphatidylcholine solutions.
**: As outlined in claim 5 of 10/750,390, the non-aqueous ingredients are mixed first before dilution with 44% w/w water.

It would have been recognized by one of ordinary skill in the art that the claimed invention is an obvious variation of the invention set forth in claims 1-10 of copending Application No. 10/750,390 because of the common features and elements set forth in the claims analysis table above. One of ordinary skill in the art would have produced the phosphatidylcholine carrier of the instant application by the method of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-26 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EVA

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